REMARKS

Applicants respectfully request consideration of the foregoing amendments and the following comments upon continued examination of the present application on the merits.

I. Status of the Claims

Claims 1 and 35-37 have been amended to recite ***solid*** particles of beclomethasone and budesonide. Exemplary support can be found in original claim 11, which recites that the particles are crystalline, semi-crystalline, amorphous, semi-amorphous, or a mixture thereof. As one skilled in the art knows, crystalline or amorphous describes the physical state of solid particles because liquid or gas cannot be in a crystalline or an amorphous state.

Because no new matter is introduced, Applicants respectfully request entry of this amendment. Upon entry, claims 1-7, 9-11 and 13-37 will be pending, with claims 15-34 withdrawn from examination.

II. Rejection of Claims under 35 U.S.C. §103(a)

Claims 1-7, 9-11, 13-14 and 35-37 are rejected under 35 U.S.C. §103(a) for allegedly being obvious over U.S. Patent No. 5,747,001 to Wiedmann et al. ("Wiedmann") or PCT Publication No. WO 96/25918 by Wood et al. ("Wood"), in view of U.S. Patent Application Publication No. 2007/0117862 by Desai et al. ("Desai"), and as evidenced by U.S. Patent No. 6,139,870 to Verrecchia ("Verrecchia"). Applicants respectfully traverse each ground of the rejection.

As previously submitted in the Appeal Brief, Verrecchia does not support the Examiner's position that the claimed nanoparticulate active agent composition is suitable for filtration through a 0.2 micron filter because Verrecchia relates to filtration of an emulsion which comprises two immiscible liquids. In contrast, the claimed composition is a dispersion

comprising solid particles of beclomethasone and budesonide dispersed in a liquid dispersion medium. *See* the Appeal Brief, page 13 *ff.*

In the Decision on Appeal, the Board asserts that the claim language does not distinguish the particles of the claimed invention from those of Verrecchia. Applicants have amended the claims to explicitly recite that the claimed composition comprises solid nanoparticulate beclomethasone particles, solid nanoparticulate budesonide particles, or a combination thereof, and a liquid dispersion medium. Accordingly, it is not obvious to sterilize the claimed composition which is a dispersion comprising solid particles by filtering it through a 0.2 micron filter in view of Verrecchia's teaching of filtering an emulsion comprising two immiscible liquids.

Furthermore, the Board challenged the results demonstrated in the working examples on the ground that it is unclear whether the examples with HPMC and polysorbate 80 were performed under the same process conditions. *See* the Decision on Appeal, page 12, last paragraph. Applicants respectfully submit that the Board's challenge lacks factual support.

As demonstrated in detail in the specification, the experiments in working example 1 (budesonide having tyloxapol as the surface stabilizer), example 5 (budesonide having HPMC as the surface stabilizer), and example 8 (budesonide having polysorbate 80 as the surface stabilizer) were conducted under essentially the same conditions in terms of milling machine, milling media, milling speed and milling time.

More specifically, all compositions were milled in a DYNO-Mill using 500 μm Sdy-20 polymeric milling media at 4200 rpm for a period of time, and then using 50 μm Sdy-20 polymeric milling media at 4200 rpm for an additional period of time. One skilled in the art would have understood that the milling time cannot be controlled to be exactly the same. For example, certain compositions will achieve a significant particle size reduction in the first pass within a short period, and therefore, no additional milling is required before application of the

second pass. Other compositions will not achieve significant particle size reduction during a milling process, and therefore, no additional milling will affect the particle size. The milling conditions of Examples 1, 5 and 8 are compared in the table below.

Compositions	1st pass	2nd pass
Example 1, budesonide stabilized with tyloxapol	8 hours to reduce the mean particle size to 161 nm	2 hours to further reduce the mean particle size to 80 nm
Example 5, budesonide stabilized with HPMC	4 hours to reduce the mean particle size to 128 nm	4 hours to further reduce the mean particle size to 89 nm
Example 8, budesonide stabilized with polysorbate 80	2 hours to reduce the mean particle size to 221 nm	1 hour milling did not reduce the particle size (216 nm), 2 hours milling reduced the particle size to only 192 nm

Accordingly, even when processed under the reasonably controlled conditions, Examples 5 and 8 were unable to produce nanoparticulate budesonide compositions which can be sterile filtered. In contrast, when tyloxapol is used as a surface stabilizer, the nanoparticulate budesonide composition can successfully pass through a 0.2 micron filter.

As one skilled in the art would have understood, it would be unreasonable to require that the experiments were done using the same ratio of active agent, surface stabilizer and water solvent. *See* the Decision on Appeal, page 12, last paragraph. This is because each surface stabilizer is different in terms of physical and chemical properties and its compatibility to the specific active agent. Therefore, it is impossible to test the nanoparticulate budesonide compositions using the same ratio of tyloxapol, HPMC and polysorbate 80. One skilled in the art would have understood that the experiments were done under conditions where all controllable variables were adjusted to the same level.

Accordingly, the unexpected results are sufficient rebuttal evidence to overcome the rejection under 35 U.S.C. §103(a).

CONCLUSION

The present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested. The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by the credit card payment instructions in EFS-Web being incorrect or absent, resulting in a rejected or incorrect credit card transaction, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date Nov 22, 2010

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